MMHCC
the Mouse Models of Human Cancers Consortium

MMHCC Newsletter September 2006

MouseLine

A New Platform for Cancer Research Advances

Traditionally, much of laboratory-based cancer research has focused on the inner workings of the cancer cell or a specific cancer gene. As a result, we have generated a formidable - although still incomplete - understanding of cancer cell biology.

We also now know that, although this "reductionist" approach has proven to be extremely valuable and led to important advances, we also must develop a more cohesive understanding of how cancer cells interact with, and are influenced by, their molecular and cellular environments.

In 2004, NCI launched perhaps the largest single effort to study cancer as a complex biological system by establishing the Integrative Cancer Biology Program (ICBP). Integrative cancer biology is a unique pursuit, drawing on expertise from diverse fields such as engineering, physics, and mathematics to develop predictive computational models of biological processes critical to cancer initiation, progression, and metastasis.

These predictive models, which take into account factors like molecular dynamics, cellular interactions, and organ and tissue interaction, will serve to generate hypotheses that will form the basis for further experimental designs in the lab and clinic.

The ICBP is composed of programs at nine research centers. At these centers, interdisciplinary research teams are developing computational models of processes such as DNA repair, gene expression and silencing, mitogenesis, and cell migration/metastasis.

Already these programs are producing important new findings. Two studies published in *Nature* earlier this year, for instance, used systems biology-based models to generate exciting findings about important signaling pathways in cancer that can help guide efforts to test agents that have molecular targets in those pathways.

Dr. Todd Golub and colleagues of the ICBP program at the Dana-Farber Cancer Institute and the Broad Institute are pioneering an exciting, cost-effective new method of drug discovery. The approach relies on a genomic signature-based screening process to identify already-characterized small molecules, including FDA-approved agents, that appear to allow a cancer cell to acquire the molecular characteristics of its normal counterpart, based on computer model predictions. Using this approach, his team discovered that gefitinib (Iressa) might be a potential treatment for acute myeloid leukemia (AML), even though AML does not express the epidermal growth factor receptor, which was thought to be gefitinib's primary target. A clinical trial testing gefitinib in patients with advanced, refractory AML has now been launched.

MouseLine cont.

In the ICBP program at the Massachusetts Institute of Technology, Dr. Doug Lauffenburger and colleagues have developed models of prostate tumor cell migration that suggest the cell's ability to infiltrate a given tissue is not necessarily a property of the cell, but of the tissue it is trying to invade and the surrounding environment. In the model, when a therapeutic agent intended to inhibit cellular invasion was introduced, it was successful in some tissue environments, but in others actually made the tumor cell highly invasive or metastatic. Clearly, studies like these will inform laboratory and clinical studies of approved therapeutics and those under development.

Importantly, education and training is a central component of ICBP, ensuring that there will be a next generation of researchers to build on the excellent work being conducted now.

I'd like to congratulate ICBP Chief Dr. Dan Gallahan and Program Directors Dr. Jennifer Couch and Betty Tarnowski, as well as Division of Cancer Biology Director Dr. Dinah Singer, for making this important program a reality. Through ICBP, NCI is facilitating the development of the integrative cancer biology field, and creating an entirely new research platform from which a host of new interventions and insights can proceed.

Dr. John E. Niederhuber
Acting Director
National Cancer Institute

Source: NCI Cancer Bulletin, August 1, 2006
http://www.cancer.gov/ncicancerbulletin/NCI_Cancer_Bulletin_080106/page3

Selected Meetings

September 10 - 17, 2006
5th Annual Workshop on the Pathology of Mouse Models for Human Disease
Seattle, Washington
For more information please contact the workshop organizer: Robert Hackman, MD (rhackman@seattlecca.org)

September 15 - 18, 2006
25th Congress of the International Association for Breast Cancer Research
Montreal, Quebec, Canada
Meeting information: http://www.iabcr.com

October 24 - 26, 2006
Cambridge Healthtech Institute's 2nd Annual: Preclinical Disease Models
Boston, Massachusetts
Meeting information: http://www.DiscoveryOnTarget.com

October 25 - 28, 2006
AACR Special Conference - Mouse Models of Cancer
Cambridge, Massachusetts
Meeting information: http://www.aacr.org/page6654.aspx

Advance Registration, Abstract Submission, and Award Application Deadline: September 17, 2006

Funding Opportunities and Notifications

Support for Mouse Metabolic Phenotyping Centers
NOT-DK-06-014
National Institute of Diabetes and Digestive and Kidney Diseases
http://grants.nih.gov/grants/guide/notice-files/NOT-DK-06-014.html

Request for Information (RFI): Proposed Change in Grant Appendix Materials
NOT-OD-06-088
National Institutes of Health
http://grants.nih.gov/grants/guide/notice-files/NOT-OD-06-088.html

Repository News

The MMHCC Mouse Repository is an NCI-supported resource for the distribution of mouse cancer models and associated strains. The Repository makes strains available to all members of the scientific community. Up to 3 breeder pairs of each available strain may be ordered.

Newly accepted strains

The following strains have recently been accepted into the MMHCC Repository and will be available for distribution soon (*please click on the specific link, below, for additional information*):

1. CD-1-Tg(Tag)12T7Rjm (12T-7f)
   http://mouse.ncifcrf.gov/details.asp?ID=01XL2
2. CD-1-Tg(Tag)12T10Rjm (12-T10)
   http://mouse.ncifcrf.gov/details.asp?ID=01XL3
3. B6.FVB-Tg(Ipfl-cre)1Tuv (Pdx-1-cre)
   http://mouse.ncifcrf.gov/details.asp?ID=01XL5
4. C57BL/6-Tg(CD2-Tgfbr2)1Grs (C57BL/6 DNTGFRII)
   http://mouse.ncifcrf.gov/details.asp?ID=01XBE
5. FVB;129S6-*Stk11* ^{tm1Rdp} (Lkb1 flox)
   http://mouse.ncifcrf.gov/details.asp?ID=01XN2

More information can be found on the Mouse Repository's website: http://mouse.ncifcrf.gov

To unsubscribe from this newsletter please send an email to Dr. Betty Tarnowski tarnowsb@mail.nih.gov Send meeting announcements and other information you would like to have included in this newsletter to Ulli Wagner: ulrike@mail.nih.gov